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Original article

CLINICAL AND DIAGNOSTIC STUDIES ON FELINE HEPATIC LIPIDOSIS AND THE SIGNIFICANCE OF miRNA-122 AS A BIOMARKER

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Summary

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Hepatic lipidosis is one of the common causes of feline hepatic disorders in cats. Data on the incidence of feline hepatic lipidosis (FHL) in cats were gathered. FHL was diagnosed through comprehensive clinical, ultrasonographic, and haemato-biochemical examinations. Moreover, hepatocyte-derived miRNA-122 evaluation was conducted. Macroanatomical study on normal and diseased livers was performed. The present study was conducted on 40 cats (20 cases suffering from hepatic lipidosis and 20 apparently healthy control cases) from different common breeds in Egypt: Persian, Himalayan, mixed, of various ages and sexes. The cats suffering from different hepatopathies were 128 of all diseased animals; out of them 20 cats suffered from FHL. FHL was mostly recorded in Persian breeds older than 3 years, more commonly in tom cats than in queens. The most commonly recorded clinical signs were generalised weakness, weight loss, yellow skin, icteric mucous membranes, and anorexia. The liver appeared large with diffused hyperechogenicity on ultrasound. The physical examination showed significant elevation in respiratory and pulse rates. Haematological evaluation of FHL cases showed anaemia with a significant decrease in PCV, red blood cell counts, haemoglobin concentration, MCH, and MCHC; along with significant increase in total white blood cell count, platelets and absolute neutrophil count. Serum biochemistry revealed significant elevation in the levels of aspartate aminotransferase (AST), total bilirubin, and direct bilirubin in addition to a significant increase in the levels of BUN, creatinine, total cholesterol, triglyceride levels and serum glucose levels. Hepatic biomarker (miRNA-122) expression was significantly increased in cats with FHL: 5.04 ± 0.16 fold. Macroanatomically, the liver of healthy cats showed uniform mostly reddish-brown coloration and was divided into six main lobes. In FHL post mortem, livers showed yellowish discoloration appearing on parts of some hepatic lobes or affecting a whole lobe or both. Hepatomegaly was a common finding in FHL livers.

Key words: feline, haemato-biochemistry hepatic lipidosis, liver macro-anatomy, miRNA-122, ultrasonography

INTRODUCTION

The feline liver is considered the largest internal organ in the body, that occupies about 3–4% of total body weight. It consists of four lobes, four sub-lobes, and two processes (Otte *et al.*, 2017; Miyazaki *et al.*, 2019).

Feline hepatopathies are considered as common disorders facing small animal practitioners. Their etiology and clinical presentation are different from those of dogs. The most common disorders in cats are more related to the biliary tree and gallbladder than to hepatic tissue-related disorders as in dogs. Parenchymatous disorders are commonly associated with systemic diseases while the biliary system is the main target for infectious and non-infectious causes (Otte *et al.*, 2017; Nelson & Couto, 2019; Jaffey, 2022).

In feline patients, non-infectious causes of inflammatory liver diseases are more prevalent than infectious causes (Clark *et al.*, 2011). The most encountered causes of feline hepatic disorders might be infiltrative diseases such as hepatic lipidosis (Fluen *et al.*, 2019). The disease is defined by an excessive accumulation of triglycerides in more than 80% of hepatocytes which can result in marked increase in liver weight, function disability, and intra-hepatic cholestasis (Valtolina & Favier, 2017; Valtolina, 2019). Clinical presentation of feline hepatopathies is commonly inconsistent and might be misdiagnosed in some cases. Clinical signs are nonspecific like anorexia, lethargy and vomiting. More specific signs such as jaundice and cranial abdominal pain are commonly presented in cases with biliary tract disease associated with pancreatitis. These challenging clinical signs occurred due to the close association between hepatic and pancreatic disorders (Nelson & Couto, 2019).

The diagnosis of feline hepatopathies depends on a battery of laboratory investigations as haematology tests that examine liver cell integrity and others that test liver functions. The serum biochemical profile is specific in evaluating the integrity of hepatocytes and the biliary system including serum liver enzymes. Also, other serum parameters including serum albumin, urea, bilirubin, cholesterol, and glucose levels are investigated. The lipid profile is another group of tests that could be considered biomarkers for feline hepatic lipidosis. Laboratory criteria include low HDL and high LDL levels toward the normal reference ranges (Webb, 2018; Minamoto *et al.*, 2019).

Available serum biochemical profiles might be inconclusive in some situations, explaining the need for new specific and sensitive diagnostic biomarkers. A novel biomarker for diagnosis of feline hepatopathies including hepatic lipidosis is the estimation of serum concentrations of hepatic-derived micro-RNA-122. It was considered useful and specific biomarker for organ damage due to its considerable stability, easy assessment in biological fluids and tissue specificity (Koenig *et al.*, 2016; Armstrong *et al.*, 2022). MicroRNAs (miRNAs) are considered prospective beneficial biomarkers of hepatic injury in both acute and chronic conditions. These short non-coding RNAs are extremely durable and stable in all body fluids including blood. MiRNAs are released into the extracellular space in a stress-specific way and circulate in distinct compartments, such as protein complexes and extracellular vesicles (Arrese *et al.,* 2015, Koenig *et al.,* 2016). Estima-

tion of the serum hepatic-derived microRNA-122 is considered as a novel biomarker for diagnosis of feline hepatopathies (Armstrong *et al.*, 2022).

The main objective of our study was to estimate the incidence of feline hepatic lipidosis in cats at the Teaching Veterinary Hospital, Faculty of Veterinary Medicine, Cairo University, Egypt. This study aimed also to identify selected risk factors, haematobiochemical alterations, as well as the utility of hepatocyte-derived miRNA-122 in the diagnosis of feline hepatic lipidosis.

MATERIALS AND METHODS

Ethical approval

All research procedures were approved by the Institutional Animal Care and Use Committee, Cairo University with approval number (Vet-CU-IACUC No. 18042024907).

Animals

In the current study, 40 cats admitted to the Teaching Veterinary Hospital, Faculty of Veterinary Medicine, Cairo University, and private clinics belonging to the Giza governorate (July 2023 to July 2024) were enrolled. All cats were from different common breeds (Persian, Himalayan, and mixed breeds) and of various ages. The present study was conducted on 20 cases suffered from hepatic lipidosis and 20 apparently healthy control cases.

The macroanatomical study was constructed on 6 cats of different age and sex; 3 cats from the control group and another 3 from the group clinically diagnosed with hepatic lipidosis, referred freshly dead from accidents or disease to the anatomy lab, from the Veterinary Clinic of the Faculty of Veterinary medicine, Cairo University.

Clinical examination

Admitted cases were recorded in the registration sheet for date, age, breed, and the main complaints reported by owners. A comprehensive clinical examination including history (medical, vaccination, dietary, management, and environmental) was taken. Vital signs were assessed. Different systems and organs were carefully investigated (Rijnberk & van Ooijen, 2009).

Ultrasonographic examination

Trans-abdominal ultrasonography was done for the evaluation of hepatic parenchyma, blood vessels, biliary system, gallbladder, and other abdominal organs by using the E-Saote® ultrasonographic device equipped with a micro-convex transducer (5−10 MHz) according to Nyland & Mattoon (2002).

Hemato-biochemical and hepatocyte-derived miRNA-122 evaluation

Whole blood samples were obtained from the cephalic or jugular vein of all cats in in tubes containing EDTA to estimate the haematological parameters and in plain tubes for serum separation and quantification of total protein, albumin, globulin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), total, direct bilirubin, BUN, creatinine, sodium, potassium, chloride, total cholesterol, HDL, LDL, triglycerides and glucose using specific test kits according to manufacturer instructions (Spectrum diagnostic Co., MDSS, GmbH, Hannover, Germany). Serum samples were stored at −80 ºC till hepatocyte-derived miRNA-122 was analysed. RNA from samples was extracted using RNeasy

Mini Kit (Cat. No. 74104, QIAGEN, Germany) according to manufacturer instructions (Li *et al.*, 2012; Chen *et al.*, 2013).

Quantitative polymerase chain reaction (PCR) was applied for the detection of hepatocyte-derived miRNA-122 using the Quantitect SYBR Green PCR Kit (QIAGEN, Germany). Oligonucleotide primers and probes used in SYBR Green Real-time PCR are shown in Table 1 and cycling conditions for SYBR Green Real-time PCR are described in Table 2. The amplification curves and cycle threshold (CT) values were determined by the Stratagene MX3005P software (Yuan *et al.*, 2006). The variation of gene expression on the RNA of the different samples was estimated by the CT of each sample and compared with that of the apparently healthy control group.

Faecal analysis

Stool samples of each case was collected and examined soon during the examination. Gross appearance, direct smear, and concentration floatation technique were applied for the presence of adult worms, parasitic eggs and protozoa oocyte (Zajac & Conboy, 2012).

Anatomical study

Through mid-laparotomy along the *linea alba*, the abdominal cavity was exposed to carry on post mortem investigation on the liver *in situ* and separated, followed by fixation by arterial perfusion with 10% neutral buffered formalin. The specimens were photographed in each step performed. The anatomical nomenclature used in this study was in accordance with (NAV, 2017).

Statistical analysis

All quantitative data of haematology and serum biochemistry tests were presented as mean ± standard error. The comparison between the control and the diseased group was made by the Student *t*-test

Table 1. Oligonucleotide primers and probes used in SYBR Green real time PCR

Reference gene	Primer sequence (5'-3')	Gene
U6 (housekeeping)	GCTTCGGCAGCACATATACTAAAAT CGCTTCACGAATTTGCGTGTCAT	(Chen *et al.*, 2013)
miRNA-122	GCGAGCACAGAATTAATACGAC TGGAGTGTGACAATGGTGTTTG	(Li *et al.*, 2012)

Table 2. Cycling conditions for SYBR Green Real-time PCR according to Quantitect SYBR Green PCR Kit

		U6 housekeeping gene	miRNA-122 gene
Reverse transcription		50 °C; 30 min.	
Primary denaturation		94 °C; 15 min.	
Amplification (40 cycles)	secondary denaturation	94 °C; 15 sec.	
	annealing	60 °C; 30 sec.	55 °C; 30 sec.
	extension	72 °C; 30 sec.	
Dissociation curve (1 cycle)	secondary denaturation	94 °C; 1 min.	
	annealing	60 °C; 1 min.	55 °C; 1 min.
	final denaturation	94 °C; 1 min.	

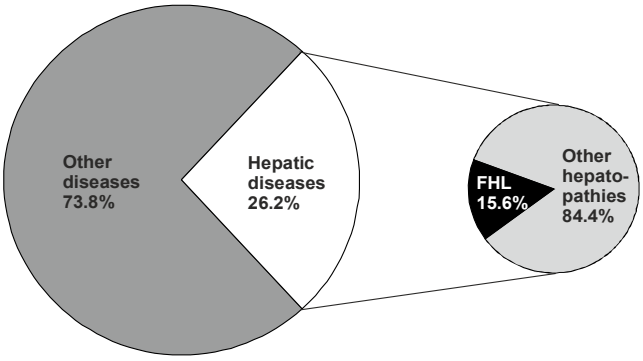

Fig. 1. Incidence of feline hepatic diseases and feline hepatic lipidosis at the Teaching Veterinary Pet Animal Hospital, Faculty of veterInary Medicine, Cairo University, Egypt during the study period (July 2023–July 2024).

Table 3. Incidence of feline hepatic lipidosis in cats admitted to the Teaching Veterinary Hospital, Faculty of Veterinary Medicine, Cairo University for one year period study from July 2023 to July 2024

Group	Apparently healthy cats	Diseased cats		
Sub-group		Hepatopathies		Other health problems
Common causes		Feline hepatic lipidosis	Other causes of hepatopathies	360 (73.8%)
No. (%)	231(32.1%)	20 (15.6%)	108 (84.3%)	
		128 (26.2%)		

(SPSS v. 16.0); P≤0.05 was considered statistically significant (George & Mallery, 2019).

RESULTS

Records showed that hepatopathies were detected in 128 cases (26.2%) of all 488 diseased cats admitted to the Teaching Veterinary Pet Animal Hospital, Faculty of Veterinary Medicine, Cairo University, Egypt from July 2023 to July 2024 (Fig. 1). Feline hepatic lipidosis was detected in 20 cases (15.6%) out of 128 animals suffering from hepatopathies (Table 3).

Investigation of risk factors showed that feline hepatic lipidosis was mostly recorded in Persian cats older than 3 years. Disease was detected more frequently in tom cats than in queens. The majority of cases were recorded during winter months. Results illustrated that hepatic lipidosis was more prevalent in cats with free access to food than in cats on scheduled daily feeding programs. Regarding feed type, disease incidence was higher in cats that depend on mixed feed type than dry food (Table 4).

Regarding the clinical signs of lipidosis, the most recorded clinical signs were generalised weakness, weight loss, yellow skin (Fig. 2A), icteric mucous membranes (Fig. 2B,C), and yellow ear pinnae (Fig. 2D). Anorexia was the most recorded sign

Table 4. Risk factors associated with feline hepatic lipidosis through the study period (2023–2024)

Risk factors		Lipidosis (n=20)	
		Number of cases	Percentage
Breed	Persian	12	60%
	Mixed breeds	7	35%
	Siamese	1	5%
Age	Less than 2 years	3	15%
	2–3 years	1	5%
	More than 3 years	16	80%
Sex	Tom cats	14	70%
	Queens	6	30%
Season	Summer	5	25%
	Autumn	1	5%
	Winter	9	45%
	Spring	5	25%
Feeding programme	Free access	18	90%
	Scheduled	2	10%
Diet type	Dry food	6	30%
	Soft canned food	0	0%
	Fresh food (wet food)	3	15%
	Mixed type food	11	55%

in all cases. Other associated non-specific clinical signs included ptyalism, vomiting, diarrhoea, and oliguria as many of the cases suffered from secondary hepatic lipidosis associated with another disease such as gastritis (one case), enteritis (one case), chronic renal failure (4 cases), obstructive urolithiasis (9 cases) and idiopathic (5 cases).

Ultrasonographic examination was applied to the affected cases at admission time (Fig. 3). The liver appeared large with diffuse hyper-echogenicity on ultrasound. The attenuation of the ultrasound beam increased, and the poor appearance of intra-hepatic vessel borders.

All cases with feline hepatic lipidosis were subjected to thorough physical, haematological, and biochemical examination and compared with the apparently healthy control cats. Regarding physical examination, statistical results showed significant

Fig. 2. Clinical signs associated with feline hepatic lipidosis: yellow skin of the face (A), icteric mucous membrane of the eye (B), icteric mucous membrane of the mouth (C), yellow coloured ear pinnae (D).

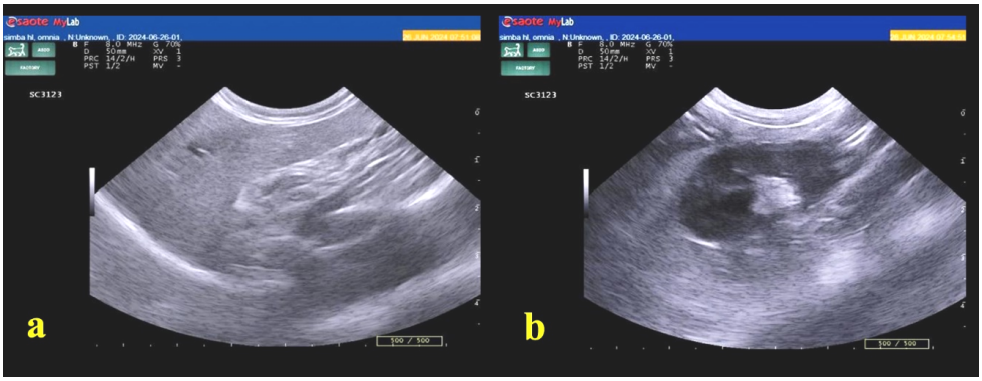

Fig. 3. Ultrasonographic view of the liver in case of feline hepatic lipidosis: hyper-echogenic hepatic tissue with poor visualisation of hepatic vessels (A); enlarged liver that put pressure on the right kidney (B).

Table 5. Physical examination parameters (mean ± SEM) in cats suffering from hepatic lipidosis (FHL).

Physical parameters	Control group (n=20)	FHL group (n20)
Respiration rate (min^{-1})	47.7 ± 2.44	95.0 ± 2.58***
Pulse rate (min^{-1})	156.0 ± 2.22	192.0 ± 3.68***
Rectal temperature (°C)	38.6 ± 0.07	38.7 ± 0.11

*P≤0.05, **P≤0.01, ***P≤0.001.

(P≤0.001) elevation in respiratory and pulse rates while there was no significant change in rectal temperature (Table 5).

In terms of haematological evaluation, the results showed a significant decrease in packed cell volume, red blood cell counts (P≤0.01), haemoglobin concentration (P≤0.001), MCH and MCHC (P≤0.05) in FHL cases compared with the apparently healthy control group. Results also showed a significant increase in white bood cell and platelet counts (P≤0.01), and absolute neutrophil count (P≤0.05). A complete blood count (CBC) showed anaemia of slight macrocytosis and hypochromacia. Other parameters had no significant changes (Table 6).

Regarding serum biochemical parameters of hepatic function, statistically significant elevation in the levels of aspartate aminotransferase (P≤0.01), total bilirubin (P≤0.001), and direct bilirubin (P≤0.05) toward apparently healthy cats was demonstrated. Renal function tests revealed a significant increase in the levels of BUN (P≤0.001) and creatinine (P≤0.05) in affected cats. Electrolyte profile results showed a significant decrease in potassium (P≤0.01) and chloride (P≤0.001) in diseased cats. The lipid profile was characterised with a significant increase in total cholesterol and triglyceride levels (P≤0.05). The same significant increase (P≤0.05) was recorded for serum glucose level (Table 7).

The fold expression of the hepatic biomarker miRNA-122 recorded a high significant (P≤0.001) increase in cats with

Table 6. Haematological parameters (mean ± SEM) in cats suffering from hepatic lipidosis (FHL)

Haematological parameters	Control group (n=20)	FHL group (n=20)
Packed cell volume (%)	38.3 ± 1.18	30.9 ± 2.15**
Hb (g/L)	136.0 ± 5.6	99.0 ± 8.40***
RBCs count (T/L)	8.9 ± 0.33	7.17 ± 0.52**
MCV (fL)	43.0 ± 0.78	43.6 ± 0.87
MCH (pg/L)	15.2 ± 0.42	13.6 ± 0.53*
MCHC (%)	35.3 ± 0.88	31.5 ± 1.35*
WBCs count (G/L)	10.6 ± 0.90	15.6 ± 1.45**
Absolute neutrophils (G/L)	5.9 ± 0.45	8.9 ± 1.12*
Absolute lymphocytes (G/L)	3.3 ± 0.48	4.8 ± 0.91
Absolute monocytes (G/L)	0.35 ± 0.12	0.74 ± 0.23
Absolute eosinophils (G/L)	0.61 ± 0.13	0.84 ± 0.27
Absolute basophils (G/L)	0.23 ± 0.04	0.12 ± 0.04
Platelet count (G/L)	343.6 ± 19.0	544.7 ± 60.9**

*P≤0.05, **P≤0.01 and ***P≤0.001.

Table 7. Serum biochemical parameters (mean ± SEM) in cats suffering from hepatic lipidosis (FHL)

Serum parameters	Control group (n=20)	FHL group (n=20)
Total proteins (g/L)	77.4 ± 5.1	74.0 ± 5.5
Albumin (g/L)	32.0 ± 1.4	32.0 ± 2.6
Globulins (g/L)	46.0 ± 4.1	42.0 ± 4.00
A/G ratio	0.83 ± 0.11	0.88 ± 0.08
Aspartate aminotransferase (IU/L)	40.1 ± 4.00	58.3 ± 4.94**
Alanine aminotransferase (IU/L)	67.0 ± 5.94	97.3 ± 15.94
Alkaline phosphatase (IU/L)	41.5 ± 4.83	51.9 ± 5.13
Gamma-glutamyl transferase (IU/L)	3.4 ± 0.66	5.3 ± 1.16
Total bilirubin (µmol/L)	3.07 ± 0.34	12.6 ± 2.05 ***
Direct bilirubin (µmol/L)	1.36 ± 0.17	4.10 ± 1.02*
BUN (mmol/L)	9.57 ± 1.03	23.6 ± 3.42 ***
Creatinine (µmol/L)	96.3 ± 4.42	318.3 ± 86.6 *
Sodium (mEq/L)	135.0 ± 5.10	134.3 ± 9.22
Potassium (mEq/L)	3.9 ± 0.36	2.6 ± 0.28**
Chloride (mEq/L)	98.2 ± 4.19	76.2 ± 4.02***
Triglycerides (mmol/L)	0.74 ± 0.08	1.20 ± 0.23*
Total cholesterol (mmol/L)	3.47 ± 0.22	4.11 ± 0.13*
HDL (mmol/L)	2.24 ± 0.15	1.88 ± 0.16
LDL (mmol/L)	1.84 ± 0.09	2.17 ± 0.25
Glucose (mmol/L)	6.42 ± 0.17	7.88 ± 0.62*

*P≤0.05, **P≤0.01 and ***P≤0.001.

hepatic lipidosis compared with apparently healthy control group (Table 8).

In the gross anatomical study, the liver in healthy cats showed uniform coloration mostly reddish-brown in fresh specimens (Fig. 4A). It was situated in the intrathoracic part of the abdominal cavity closely in contact with the diaphragm to which it adhered by 4 sets of parietal attachments; left and right coronary ligaments and left and right triangular ligaments. On the other hand, feline lipidosis also known as fatty liver syndrome (Fig. 4B), is a frequent disease in cats of different age groups, mostly caused as a complication to other underlying conditions. Also, hepatomegaly was a common finding in diseased cats, considering that the hepatic ventral border extended into the abdominal cavity far beyond the right and left costal arches, where the liver is not conformed into the intrathoracic part of the abdominal cavity as compared to livers in healthy cats (Fig. 4B).

Cat liver was divided into six main lobes assembled at the *porta hepatis* and well separated by deep interlobar fissures (Fig. 5A). These lobes are the right and left lobes which divided the organ into lateral and medial sections; the left medial

Table 8. Serum hepatocyte-derived miRNA-122 analysis.

	U6 cycle threshold	MiRNA-122 CT cycle threshold	Fold change (mean ± SEM)
Control healthy group	20.12	23.39	1.00 ± 0.00
Feline hepatic lipidosis group	21.19	22.13	5.04 ± 0.16***

***P≤0.001 vs control group.

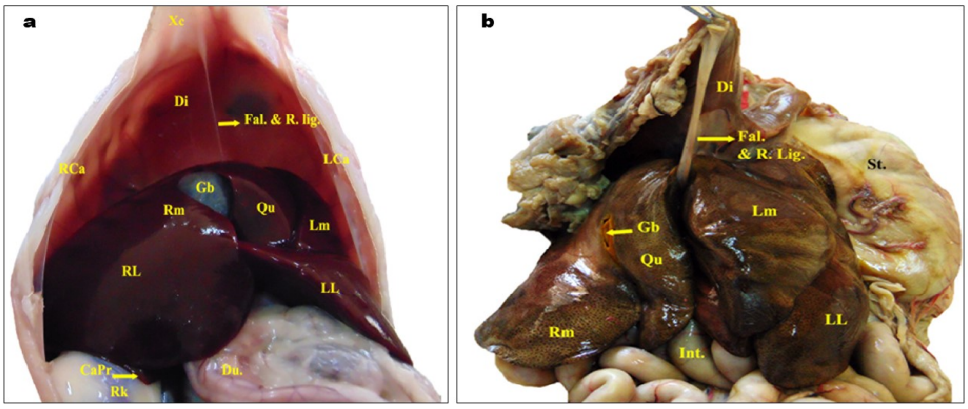

Fig. 4. A photograph showing the position, shape, and size of normal healthy (A) and diseased (B) feline liver (both freshly dissected). Notice signs of hepatomegaly and discoloration in hepatic lipidosis. *Xc*: xyphoid cartilage, *RCa*: right costal arch, *LCa*: left costal arch, *Di*: diaphragm, *Fal.* & *R.lig.*: falciform and round ligaments, *CaPr*: caudate process of caudate hepatic lobe, *RL*: right lateral hepatic lobe, *Rm*: right medial hepatic lobe, *Qu*: quadrate hepatic lobe, *Lm*: left medial hepatic lobe, *LL*: left lateral hepatic lobe, *Gb*: gall bladder, *St.*: stomach, *Du.*: duodenum, Int.: intestine, *RK*: right kidney.

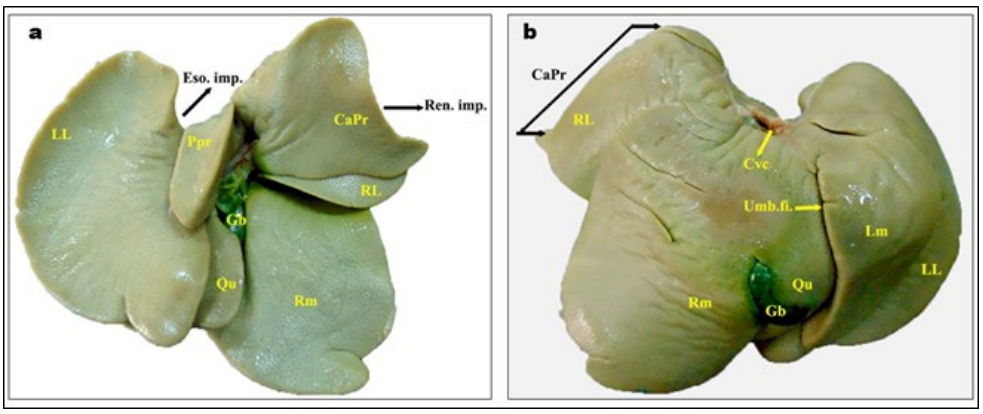

Fig. 5. A photograph showing the normal appearance and lobation of the formalised cat liver: the visceral surface (A) and the parietal surface (B). *CaPr*: caudate process of caudate hepatic lobe, *Ppr*: papillary process of caudate hepatic lobe, *RL*: right lateral hepatic lobe, *Rm*: right medial hepatic lobe, *Qu*: quadrate hepatic lobe, *Lm*: left medial hepatic lobe, *LL*: left lateral hepatic lobe, *Gb*: gall bladder, *Eso.imp.*: esophgeal impression, *Ren.imp.*: renal impression, *Cvc*: caudal vena cava, *Umb.fi.*: umbilical fissure.

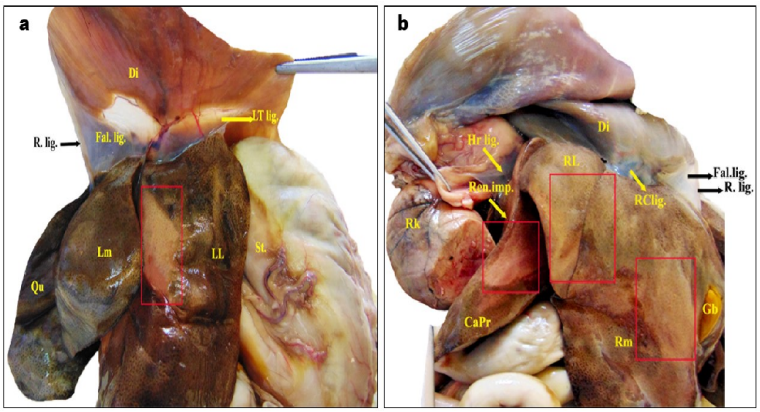

Fig. 6. A photograph showing signs of feline hepatic lipidosis (red windows) on left (A) and right (B) hepatic lobes. *Di*: diaphragm, *Fal.lig.*: falciform ligament, *R. lig.*: round ligament, *LTlig.*: left triangular ligament, *Hr lig.*: hepatorenal ligament, *RClig.*: right coronary ligament, *CaPr*: caudate process of caudate hepatic lobe, *RL*: right lateral hepatic lobe, *Rm*: right medial hepatic lobe, *Qu*: quadrate hepatic lobe, *Lm*: left medial hepatic lobe, *LL*: left lateral hepatic lobe, *Gb*: gall bladder, *Ren.imp.*: renal impression, *St.*: stomach, *RK*: right kidney.

lobe was separated from the quadrate lobe by a deep umbilical fissure (Fig. 5B), and finally the caudate lobe subdivided into caudate and papillary processes, the caudate process on the right side holding a renal impression embracing the right kidney and being attached through the hepatorenal ligament. The gall bladder is positioned in the fossa between the right medial and quadrate lobes. All lobes appeared on the hepatic visceral surface except the left medial one (Fig. 5A).

Either way, in postmortem assessment, affected livers showed signs of jaundice

with yellowish discolorations appearing on parts of some hepatic lobes or affecting a whole lobe or both lobes, according to the degree of hepatic affection (Fig. 6).

DISCUSSION

Regarding the incidence of feline hepatic lipidosis (FHL), this study revealed that it was detected in 15.6% of cases suffering from hepatopathies as also stated by Hirose *et al.* (2014). On the contrary, hepatic lipidosis prevalence was reported at 7.6% of all submissions in other studies (Bayton *et al.*, 2018; Fluen *et al.*, 2019). Also, 26.2% of collected diseased cases suffered from hepatopathies, in contrast to reported data by Melchert *et al.* (2016) where hepatic disorders recorded 7% of total diseased cases.

The present study showed that feline hepatic lipidosis was mostly recorded in the Persian breed (Kelany *et al.*, 2009), and the predilection age was over 3 years, in line with (Hirose *et al.*, 2014) who mentioned a median age of 11 years, and opposite to other data (Center, 2005; Valtolina & Favier, 2017) affirming that FHL had no exact breed or gender predilection and cats of any age can be affected.

FHL was detected more frequently in tom cats than in queens, contrary to the study of Hirose *et al.* (2014) where the male to female ratio of lipidosis was 1:2. Our study detected that most cases were recorded during the winter months due to the higher occurrence of negative energy balance during this season.

FHL is categorised as idiopathic, or might appear as a result of anorexia which occurs most frequently in overweight cats (Webb, 2018) following our results. In addition, common detected causes of HL were gastritis, enteritis, chronic renal failure, and obstructive urolithiasis. Regarding the clinical signs of FHL, the most commonly recorded clinical signs were generalised weakness, weight loss, yellow skin, icteric mucous membranes, yellow ear pinnae and anorexia. Other associated non-specific clinical signs included ptyalism, vomiting, diarrhoea as previosuly reported (Valtolina & Favier, 2017; Valtolina, 2019; Webb, 2018; Nelson & Couto, 2019).

In accordance with other published data (Valtolina & Favier, 2017; Heo *et al.*, 2018; Valtolina, 2019), the ultrasonographic examination showed that the liver was large with diffused hyper-echogenicity on ultrasound, increased attenuation of the ultrasound beam, and poor appearance of intra-hepatic vessel borders.

In agreement with Johnson (2018) and Ryan *et al.* (2019), physical examination results showed a significant elevation in respiration and pulse rates.

Our study's complete blood count (CBC) findings demonstrated anaemia with slight macrocytosis and hypochromacia in line with Nelson & Couto (2019), but in contrast to other studies (Valtolina & Favier, 2017; Heo *et al.*, 2018), stating that cats with FHL frequently had normal CBC. Regarding serum biochemical parameters, the results from hepatic function tests showing significant elevation in the levels of AST, total bilirubin, and direct bilirubin concurred with earlier findings (Webb, 2018; Nelson & Couto, 2019). Cats with FHL exhibited elevation in ALP, ALT activities, and total bilirubin in agreement with (Heo *et al.*, 2018). BUN and creatinine levels were significantly higher, which might be due to renal affection, opposing to data of Kelany *et al.*, (2009) that serum glucose and BUN were significantly decreased and serum creatinine was not significantly changed. The lipid profile showed a significant increase

in total cholesterol, and triglyceride levels, also serum glucose levels were significantly increased as the reported by Webb (2018) and Nelson & Couto (2019).

The present findings about the fold expression of the hepatic biomarker miRNA-122 recorded a high significant increase in cats with hepatic lipidosis, in accordance of earlier reports of diagnosing feline hepatic illness (Armstrong *et al.*, 2022), cases of liver damage in dogs (Koenig *et al.*, 2016), some hepatic affections of dogs (Eman *et al.*, 2018), and liver steatosis or fibrosis (El-Sebaey & Abramov, 2022).

The healthy liver in cats was a six lobed gland, situated in the intrathoracic part of the abdominal cavity caudal to the diaphragm, extending ventrolaterally beyond the xiphoid cartilage bordered by both costal arches to contact the ventral and lateral abdominal walls in addition to the right kidney at the renal fossa (Kealy *et al.*, 2010; Maher *et al.*, 2020). However, in cases of feline hepatic lipidosis, studies revealed the concomitant incidence of hepatomegaly alongside traces of jaundice showing up in hepatic parenchyma (Center *et al.*, 1993; Center, 2005; Webb, 2018), as our observations in the current study. Even though we agreed with Webb (2018) that hepatomegaly alone was a relatively non-specific subjective finding, further investigations are needed to determine the exact cause for management.

CONCLUSIONS

The present study spots light on hepatic lipidosis as a common hepatopathy affecting cats. Hepatopathies occurred in about 26% of diseased cats admitted to the Teaching Veterinary Pet Animal Hospital, Faculty of Veterinary Medicine, Cairo University, Egypt. FHL share of all hepatopathies was 15.6%. Occurrence of the disease was the highest in the Persian breed, at age more than 3 years, tom cats, during the winter months, cats having free access to feed and mixed type feeding. From examination and laboratory data, FHL led to hepatocellular injury expressed by concomitant elevation of white blood cell counts, neutrophils, liver enzymes and miRNA-122 levels which were specific and early predictors of inflammatory reactions of varying degrees. This made miRNA-122 a major clinically significant marker in diagnosis of hepatopathies.

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